

LISTING OF CLAIMS

1. (Cancelled).
2. (Previously amended) The method of claim 68, wherein the animal is a human.
3. (Previously amended) The method of claim 2, wherein the short-term formulation of interferon is selected from natural or recombinant alpha, beta, consensus, gamma, leukocyte, omega, or tau interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.
4. (Original) The method of claim 3, wherein the interferon-responsive disease is selected from viral hepatitis C, viral hepatitis B, condyloma accuminata, hairy cell leukemia, malignant melanoma, follicular lymphoma, AID's related Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, and tuberculosis.
5. (Currently amended) The method of claim 3, wherein the interferon-responsive disease is selected from viral hepatitis C, viral hepatitis B, condyloma accuminata, hairy cell leukemia, malignant melanoma, follicular lymphoma, AID's related Kaposi's sarcoma and the at least one interferon is selected from natural or recombinant alpha, consensus, leukocyte, omega or tau interferon or versions thereof to which polyethylene glycol or a polyethylene glycol-fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.
6. (Currently amended) The method of claim 3, wherein the interferon-responsive disease is selected from chronic granulomatous disease, pulmonary fibrosis, and tuberculosis and the at least one interferon is natural or recombinant gamma interferon or a version thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding.
7. (Currently amended) The method of claim 3, wherein the disease is multiple sclerosis and at least one ~~the~~ interferon is selected from natural or recombinant alpha, beta, consensus, leukocyte, omega or tau interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

8. (Original) The method of claim 3, wherein the same interferon is administered in the short-term formulation as is administered in the subsequent long-term formulation of interferon.
9. (Original) The method of claim 2, wherein a first interferon is administered as a short-term formulation and a different interferon is subsequently administered in the long-term formulation.
10. (Currently amended) The method of claim 2, wherein the short-term formulation and the long-term formulation are the same formulation.
11. (Currently amended) The method of claim 2, wherein the short-term formulation ~~and~~ differs from the long-term formulation ~~are two different formulations~~.
12. (Previously amended) The method of claim 2, wherein more than one interferon is administered for short-term use, each interferon being in the same formulation or in different short-term formulations.
13. (Currently amended) The method of claim 2, wherein more than one interferon is administered for long-term use, each interferon being ~~with~~ in the same formulation or ~~with~~ in different long-term ~~formulation~~ formulations.
14. (Currently amended) The method of claim 2, wherein ~~the~~ there is an overlap of administration of the short-term formulation ~~is administered first~~ and the long-term formulation is ~~subsequently administered either with or without an overlap of dosing with the short term and long term formulations~~.
15. (Original) The method of claim 2, wherein the controlled release dosage per time unit selected for the long-term formulation is about equivalent to the dosage release over the time unit for the short-term formulation.
16. (Original) The method of claim 2, wherein the controlled release dosage per time unit selected for the long-term formulation is different than that administered with the short-term formulation.

17. (Previously amended) The method of claim 2, wherein the short-term formulation is delivered by an injection, an infusion, an implantable system, a transdermal delivery system, an oral formulation, non-oral parenteral formulation, or an inhalational device.

18. (Cancelled).

19. (Twice amended) The method of claim ~~68~~ 13, wherein at least one of the long-term ~~formulation~~ formulations of interferon is selected from ~~naturally-occurring~~ natural or recombinant alpha, beta, consensus, gamma, leukocyte, omega, or tau interferon, or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

20. (Twice amended) The method of claim ~~2~~ or 19, wherein the interferon is natural or recombinant omega interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

21. (Cancelled).

22. (Previously amended) The method of claim ~~74~~, wherein the animal is a human.

23. (Cancelled).

24. (Original) The method of claim 22, wherein the interferon-responsive disease is selected from viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata, hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer, colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, and tuberculosis.

25. (Currently amended) The method of claim 22, wherein the interferon-responsive disease is selected from viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata, hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's

lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer, colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma, and ~~the~~ at least one interferon is selected from natural or recombinant alpha, consensus, leukocyte, omega or tau interferon or versions thereof to which polyethylene glycol or glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding.

26. (Currently amended) The method of claim 22, wherein the interferon-responsive disease is selected from chronic granulomatous disease, pulmonary fibrosis, and tuberculosis and ~~the~~ at least one interferon is natural or recombinant gamma interferon or a version thereof to which polyethylene glycol or glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding.

27. (Currently amended) The method of claim 22, wherein the disease is multiple sclerosis and ~~the~~ at least one interferon is selected from natural or recombinant alpha, beta, consensus, leukocyte, omega or tau interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

28. (Original) The method of claim 22, wherein the same interferon is administered in the short-term formulation and in the long-term formulation.

29. (Original) The method of claim 22, wherein a first interferon is administered as a short-term formulation and a different interferon is administered as the long-term formulation.

30. (Twice amended) The method of claim 22, wherein the ~~same formulation is administered as~~ the short-term formulation and the subsequent long-term formulation are the same formulation.

31. (Currently amended) The method of claim 22, wherein the short-term formulation differs from the ~~subsequent~~ long-term formulation.

32. (Twice amended) The method of claim 22, wherein more than one interferon is administered for short-term use, each interferon being in the same formulation or in different short-term formulations.

33. (Twice amended) The method of claim 22, wherein more than one interferon is administered for long-term use, each interferon being ~~with~~ in the same or ~~with~~ in different long-term delivery systems.

34. (Cancelled)

35. (Original) The method of claim 22, wherein the controlled release dosage per time unit selected for the long-term formulation is about equivalent to the dosage release over the time unit for the short-term formulation.

36. (Original) The method of claim 22, wherein the controlled release dosage per time unit selected for the long-term formulation is different than that administered with the short-term formulation.

37. (Previously amended) The method of claim 23, wherein the short-term formulation is selected from an injection, an infusion, an implantable system, a transdermal delivery system, an oral formulation, non-oral parenteral administration, or an inhalational device.

38. (Twice amended) The method of claim 37, wherein the short-term formulation of interferon is selected from ~~naturally occurring~~ natural or recombinant alpha, beta, consensus, gamma, leukocyte, omega, or tau interferon, or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

39. (Cancelled).

40. (Twice amended) The method of claim ~~39~~ 33, wherein at least one of the long-term ~~formulation~~ formulations of interferon is selected from ~~naturally occurring~~ natural or recombinant alpha, beta, consensus, gamma, leukocyte, omega, or tau interferon, or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

41. (Previously amended) A method of manufacturing a long-term delivery device for delivering a drug over time, which method comprises

preparing a standard rate long-term delivery device designed for delivery of a drug at a relatively constant rate over time, the rate being determined to be a unit rate designed for a patient to receive a standard dosage rate to treat a disease state in the patient treatable over time by the drug, and

preparing a reduced rate long-term delivery device designed for delivery of the same drug at a relatively constant rate over time, which rate is a fraction of the standard dosage rate,

wherein each device releases the drug from an implantable pump that is not externally programmed and is suitable for internal presentation to a patient in need thereof alone or in combination with an identical device or the other device, depending on the dosage rate or fractional dosage rate determined to be appropriate for the patient.

42. (Original) The method of claim 41, wherein the rate of delivery of the drug from the reduced rate device is about fifty percent of the rate of delivery from the standard rate device.

43. (Original) The method of claim 41, which method further comprises

preparing dosing instructions for adjusting the rate of administration of the drug by employing one or a combination of devices to achieve the desired release rate of the drug for a patient depending on the patient's needs over time.

44. (Original) The method of claim 41, wherein the drug is an interferon.

45. (Original) The method of claim 44, wherein the interferon is selected from natural or recombinant alpha, beta, consensus interferon, gamma, leukocyte, omega, or tau interferon, or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

46. (Original) The method of claim 41, wherein the disease state is an interferon-responsive disease.

47. (Original) The method of claim 46, wherein the interferon-responsive disease is selected from viral hepatitis C, viral hepatitis B, viral hepatitis D, condyloma accuminata,

hairy cell leukemia, malignant melanoma, multiple myeloma, follicular lymphoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, chronic myelogenous leukemia, basal cell carcinoma, mycosis fungoides, carcinoid syndrome, superficial bladder cancer, renal cell cancer, colorectal cancer, laryngeal papillomatosis, actinic keratosis, Kaposi's sarcoma, multiple sclerosis, chronic granulomatous disease, pulmonary fibrosis, tuberculosis.

48. (Cancelled)

49. (Currently amended) The method of claim 48 45, wherein the disease is hepatitis C and the interferon is omega interferon.

50. (Currently amended) The method of claim 48 45, wherein the disease is hepatitis C and the interferon is an alpha interferon.

51. (Currently amended) The method of claim 48 45, wherein the disease is hepatitis C and the interferon is a consensus interferon.

52. (Currently amended) The method of claim 48 45, wherein the disease is hepatitis C and the interferon is a natural or recombinant interferon.

53. (Original) The method of claim 46, wherein the interferon-responsive disease is selected from chronic granulomatous disease, pulmonary fibrosis, and tuberculosis and the interferon is natural or recombinant gamma interferon or a version thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding.

54. (Currently amended) The method of claim 44, wherein the disease is multiple sclerosis and the interferon is selected from natural or recombinant alpha, beta, consensus, leukocyte, omega or tau interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

55-67. (Cancelled).

68. (Currently amended) A method for the treatment of an interferon-responsive disorder in a warm-blooded animal, which method comprises:

administering to the animal at least one interferon formulated for short-term use;

adjusting the dosage with the short-term formulation to increase therapeutic response;

subsequently selecting a dosage to be administered as a long-term formulation ~~showing~~
having a controlled rate of release over time; and

thereafter administering the long-term formulation to release the interferon at a controlled rate over time;

wherein the long-term formulation of interferon is released from an internally presented implantable pump that is not externally programmed, and further wherein the short-term formulation of interferon is not released from the internally presented implantable pump from which the long-term formulation is released.

69. (Previously presented) The method of claim 68, further comprising the step of optionally adjusting the level of interferon released with an additional long-term formulation to further maximize therapeutic response.

70. (Previously presented) The method of claim 68, wherein the pump releases an interferon at a fixed rate.

71. (Previously presented) The method of claim 68, wherein the interferon is released from a plurality of internally presented implantable pumps that are not externally programmed.

72. (Previously presented) The method of claim 71, wherein each pump releases an interferon at a fixed rate.

73. (Previously presented) The method of claim 68, wherein the implantable pump is an osmotic pump.

74. (Currently amended) A method for individualizing doses of interferon in the treatment of interferon-responsive disorders in a warm-blooded animal, which method comprises

administering at least one interferon, formulated for short-term use, in a plurality of the animals;

adjusting the dosage with the short-term formulation to increase therapeutic response;

determining the most commonly identified optimal dosage over time in a sufficiently large population of the animals to define such dosage as a unit dose;

subsequently, defining a long-term formulation for delivering such dosage over time as more unit-dose or a fraction thereof, such that, in aggregate, the optimal dosage identified during dosing with the short-term formulation can be approximated with the unit-dose or fractional unit-dose combination using the long-term formulation to deliver the interferon in a controlled dose over time;

selecting a dosage to be administered to an individual animal with a long-term delivery; and

thereafter administering the long-term dosage with a long-term delivery system, wherein said long-term delivery system releases interferon from an internally presented implantable pump that is not externally programmable, and further wherein the short-term formulation of interferon is not released from the internally presented implantable pump from which the long-term formulation is released.

75. (Previously presented) The method of claim 74, further comprising the step of adjusting the dosage over time with the long-term formulation to further maximize therapeutic response.

76. (Previously presented) The method of claim 74, wherein the long-term delivery system releases interferon at a fixed rate.

77. (Previously presented) The method of claim 41, wherein the long-term delivery device is designed to deliver interferon at a fixed rate.

78. (New) The method of claim 3, wherein the long-term formulation of interferon is selected from natural or recombinant omega interferon or versions thereof to which polyethylene

glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

79. (New) The method of claim 2, wherein there is no overlap of administration of the short-term formulation and the long-term formulation.

80. (New) The method of claim 68, wherein the long-term formulation is released over a period of at least approximately one month.

81. (New) The method of claim 68, wherein the long-term formulation is released over a period of at least approximately a quarter year.

82. (New) The method of claim 22, wherein the long-term formulation of interferon is selected from natural or recombinant omega interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.

83. (New) The method of claim 45, wherein the interferon is selected from natural or recombinant omega interferon or versions thereof to which polyethylene glycol or a polyethylene glycol - fatty acid moiety has been attached by covalent or non-covalent bonding, or mixtures thereof.